

# Aging and Toxic Response: Issues Relevant to Risk Assessment

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## Abstract:

In 2002, EPA launched the *Aging Initiative* to develop a *National Agenda for the Environment and the Aging* to help guide the Agency's efforts to protect the health of older persons. Elderly people can be vulnerable to environmental challenges due to their age-altered physiological changes and exposure patterns. In addition, the presence of age-associated diseases or conditions may increase susceptibility to the harmful effects of specific agents. Therefore, special consideration of the elderly population is needed in assessing risk from exposure to environmental agents. For the document *Aging and Toxic Response: Issues Relevant to Risk Assessment*, a literature review was conducted to provide a very broad understanding of the functional, physiological, and biochemical changes that occur in elderly persons as well as the major age-associated diseases and conditions that may impact the age-related toxicokinetics and toxicodynamics of environmental agents. A few examples of biological responses to exposure to environmental agents in the elderly population are known. Several data gaps and research needs were identified that may inform the Agency's *Aging Initiative* in conducting research for better characterizing risk to the elderly population from exposure to environmental agents.

Physiological System	Physiological Changes in the Elderly
Genetic and Cellular Structure and Function	<ul style="list-style-type: none"><li>• Increased genetic damage</li><li>• Decreased rate of cellular repair</li></ul>
Nervous System	<ul style="list-style-type: none"><li>• Loss of neurons</li><li>• Decrease in brain weight</li><li>• Changes in neurotransmitter systems</li><li>• Cognitive, motor, and sensory function loss</li></ul>
Cardiovascular System	<ul style="list-style-type: none"><li>• Decrease in cardiac output</li><li>• Increase in arrhythmias</li><li>• Thickening and stiffening of arterial walls</li><li>• Diminished baroreceptor reflex</li></ul>
Gastrointestinal System	<ul style="list-style-type: none"><li>• Delayed gastric emptying</li><li>• Changes in gastric acidity</li><li>• Increased transit time through lower GI tract</li></ul>
Respiratory System	<ul style="list-style-type: none"><li>• Decline in pulmonary function</li><li>• Decrease in vital capacity</li><li>• Decreased mucociliary function</li></ul>
Hepatic System	<ul style="list-style-type: none"><li>• Decline in hepatic volume and blood flow</li><li>• Delayed hepatic regeneration</li></ul>
Renal System	<ul style="list-style-type: none"><li>• Lower renal blood flow and GFR</li><li>• Reduction in tubular secretion and reabsorption</li><li>• Sodium imbalance</li></ul>
Immune System	<ul style="list-style-type: none"><li>• Altered intracellular signaling</li><li>• Reduced apoptosis</li></ul>
Skin	<ul style="list-style-type: none"><li>• Changes in dermal barrier function</li><li>• Decreased body water loss through the skin</li></ul>
Body Mass	<ul style="list-style-type: none"><li>• Decrease in lean body mass</li><li>• Increase in percent fat content, change in fat distribution</li><li>• Decrease in total body water content</li></ul>
Musculo-Skeletal System	<ul style="list-style-type: none"><li>• Bone loss and joint deterioration</li><li>• Compression of cartilage</li><li>• Decrease in skeletal muscle mass and strength</li></ul>
Endocrine and Reproductive Systems	<ul style="list-style-type: none"><li>• Decreasing level of growth hormones</li><li>• Altered expression of reproductive hormones</li><li>• Atrophy of reproductive organs</li></ul>
Basal Metabolism	<ul style="list-style-type: none"><li>• Decreased total basal metabolic rate</li><li>• Decreased fat oxidation</li><li>• Decreased temperature regulation</li></ul>

## Age-Related Issues in Risk Assessment:

- Interindividual variability in toxicokinetics and toxicodynamics
- Changes in physiological status
- Changes in nutritional status
- Changes in disease status
- Changes in behavior patterns and exposure scenarios
- Changes in occupational status
- Changes in socio-economic status
- Geographic location (e.g., climate)
- Polypharmacy
- Cultural practices
- Early life exposures and latency of effect
- Generational exposures
- Selective mortality or survivor effect
- Generalizability of animal models to humans
- Application of uncertainty factors
- Availability and use of PBPK models

## Examples:

**Metals:** Elderly individuals are vulnerable to the health effects of heavy metals such as lead due to skeletal degeneration resulting in rapid release from bone stores, and decreased glomerular filtration rate (GFR) resulting in reduced clearance. Lead can cause decreased neurological, cardiovascular, and renal function.

**Pesticides:** Elderly individuals are vulnerable to the health effects of pesticides which have been implicated as contributors to neurodegenerative diseases, including Alzheimer's and Parkinson's diseases.

**Air Pollution:** Elderly individuals are vulnerable to the health effects of air pollution due to the reduced capacity of the respiratory and cardiovascular systems, particularly in individuals with preexisting diseases (e.g., asthma, COPD).



## Research Needs:

- A better understanding of the pathophysiological mechanisms of aging
- Increased monitoring of chronic diseases, particularly through the use of longitudinal studies
- Continued study of gene-environment interactions
- Focused research on the interactions between drugs and environmental contaminants
- More dialogue between epidemiologists and mechanistic researchers of elderly individuals
- More chemical-specific toxicity data in human epidemiological studies in the elderly population and in aged experimental animals
- Better characterization of such factors as activity patterns and microenvironments that contribute to the exposure of elderly populations to environmental agents
- More research on biomarkers related to aging, as well as exposure



<http://www.epa.gov/aging>



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